PCR #1

Reaction #1 Reaction #2 Primer #4 75 Primer #3 Primer #1 IFN-α 21a Gene IFN- α 2c Gene PCR Amplification 75 75 α 21a DNA Fragments α 2c DNA Fragments **PCR #2** IFN- α 21a IFN-α2c Reaction #1 **←** Primer #4 Primer #1 and #2 Fragments IFN-α21a 75 IFN-α2c HY1 (IFN-α Hybrid 1)

Construction of Hybrid #1

FIG. 1A

PCR #1

Reaction #1 Reaction #2 Primer #4 95 Primer #5 95 Primer #1 -Primer #6 IFN-α 21a Gene IFN- α 2c Gene PCR Amplification 95 95 α 21a DNA Fragments α 2c DNA Fragments **PCR #2** IFN-α21a IFN-α2c 95 - Primer #4 Reaction #1 Primer #1 and #2 Fragments IFN-α21a 95 IFN-α2c HY2 (IFN-\alpha Hybrid 2)

Construction of Hybrid #2

FIG. 1B

PCR #1

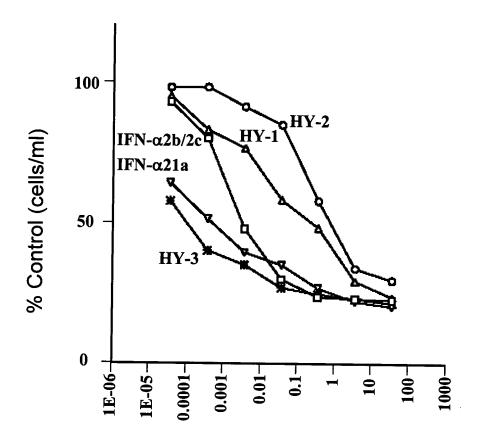
Reaction #1 Reaction #2 Primer #7 95 Primer #5 95 Primer #1 -Primer #6 IFN-α 2c Gene IFN- α 21a Gene PCR Amplification 95 95 α 2c DNA Fragments α 21a DNA Fragments **PCR #2** IFN-α2c IFN-α21a Reaction #1 - Primer #7 Primer #1 and #2 Fragments IFN-α2c IFN-α21a

Construction of Hybrid #3

HY3

(IFN-α Hybrid 3)

FIG. 1C



IFN concentration (ng/ml)

FIG. 2A

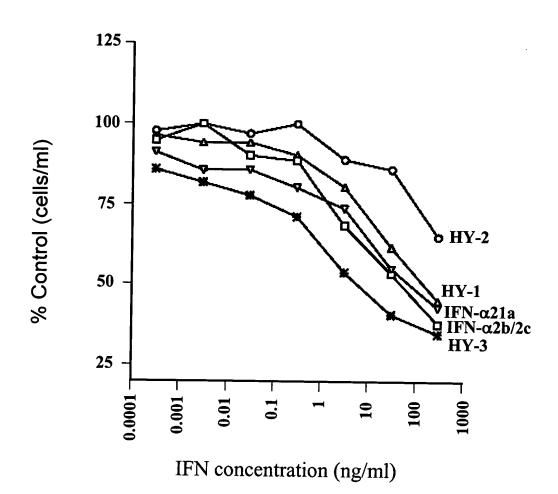


FIG. 2B

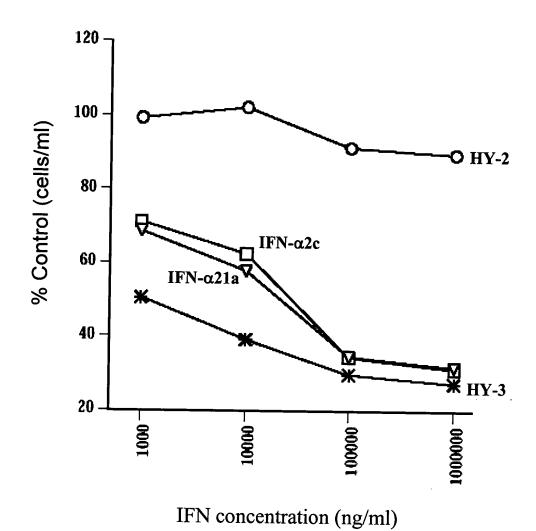


FIG. 2C

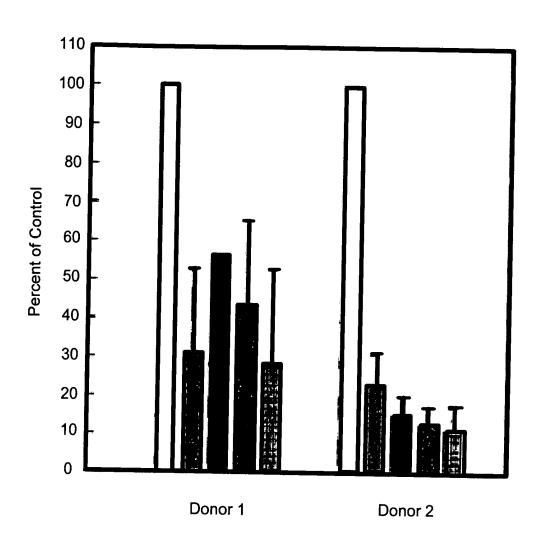


FIG. 3

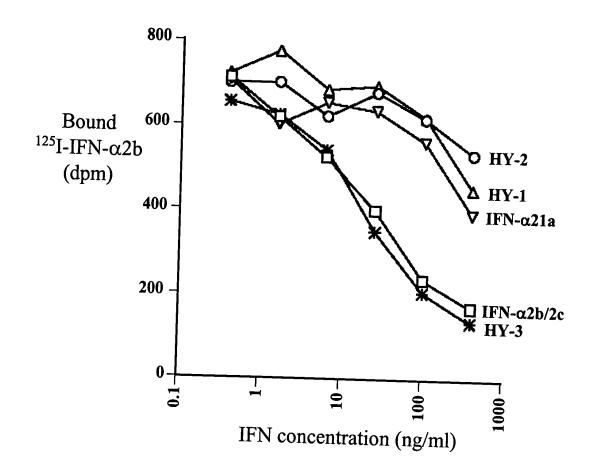


FIG. 4A

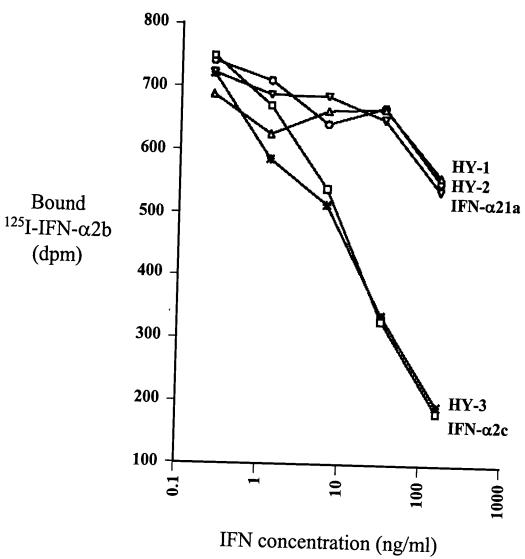


FIG. 4B

	1	2	3	4	_ 5	6	7	88	9	10	11_	12	13	14	15	16	17
Alpha 2c Alpha 21a	CC	D D	L L	P P	Q Q	T	H H	S	L L	G		R R	R R		L		L L
HY-1	C	D	L	P	Q	T	Н	S	L	G	1	R	R		L		L
HY-2 HY-3	c	D D	L L	P P	Q Q	T T	H H	s s	L L	G G		R R	R R		L L	:	L L
	18	19	20	21	22	23	24	25	26	27	28	- 29	30	31	32	33	34
Alpha 2c	L	Α	Q	M		R	I	s		F	S	С	L	K	D	R	1
Alpha 21a HY-1	L	A A	Q Q	M M	i.	R R	I	s s		F F	s s	C C	L L	K K	D D	R R	
ну-2 ну-3	L	A A	Q Q	M M		R R	I I	s s	7	F F	s s	C	L L	K K	D D	R R	45° 46
111 3						•			40		_						
Alpha 2c	35 D	36 F	37 G	38 F	39 P	40 Q	41 E	<u>42</u> E	43 F	4 4 *	45 G	46 N	47 Q	48 F	49 Q	50 K	51 A
Alpha 21a HY-1	D D	F F	G G	F F	P P	Q Q	E E	E E	F F	Q Q	G G	N N	Q	F F	Q Q	K K	A A
HY-2	D	F	G	F	P	Q	E	E	F	D	G	N	Q	F	Q	K	A
HY-3	D	F	G	F	P	Q	E	E	F	*	G	N	Q	F	Q	K	A
Alpha 2c	52	53	54 I	55 *	56 V	57 L	58 H	59 E	60 M	61 I	62 Q	63 Q	64	65 F	66 N	67 L	68 F
Alpha 21a HY-1	2.2		I	4	V V	L L	H H	E E	M M	I	Q Q	Q Q	# # #	F	N N	L L	F F
HY-2	13		Ι	ş3	V	L	Н	E	M	I	Q	Q	ii.	F	N	L	F
нү-3	;	37	Ι		V	L	Н	Е	M	Ι	Q	Q	<u>.</u>	F	N	L	F
Alpha 2c	69 S	70 T	71 K	72 D	73 S	74 S	75 A	76 *	77 W	78 (8)	79	80	81 L	82 L	83	84 K	85 F
Alpha 21a	s	T	K	D	S	S	Α	X	₩	諨			L	L	at .	K	F
HY-1 HY-2	S	T T	K K	D D	s s	S S	A A	14	W	37 64			L L	L L	2 4	K K	F F
HY-3	S	T	K	D	s	S	A	`	W	3)	÷		L	L	¥.	К	F
21-1-0-	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102
						_		 -									
Alpha 2c Alpha 21a	3	T T	E E	L L	3	Q Q	Ω Q	L L	N N	D D	L L	E	A	C C	V V	I	Q
Alpha 21a HY-1	***	T T	E E	r r	4.	Q Q	Q Q	L L	N N	D D	L L	E E	A A	C	v v	I I	Ω Ω Ω
Alpha 21a	20	T	E	L	3	Q	Q	L	N	D	L	E	A	С	V	I	Q Q
Alpha 21a HY-1 HY-2 HY-3	103	T T T T	E E E E	L L L L	107	Q Q Q Q Q	Q Q Q Q Q	L L L L	N N N N	D D D D	L L L L	E E E E	A A A A	C C C C	V V V V	I I I I	Q Q Q Q Q Q
Alpha 21a HY-1 HY-2	60 Jan 180 (Sa	T T T	e e e	L L L	* * * * *	Q Q Q Q	Q Q Q Q	L L L	N N N	D D D	r r r	E E E	A A A	с с с	v v v	I I I	Q Q Q Q Q Q 119
Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1	103	T T T T V V	E E E E G G	L L L L V V	107	Q Q Q Q 108 E E	Q Q Q Q 109 T T	L L L 110 P P P	N N N N 111 L L	D D D D 112 M M	L L L 113	E E E E	A A A A 115 D D	C C C C S S S S	V V V V 117 I I	I I I I 118 L L	Q Q Q Q Q 119 A A
Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a	103	T T T T V V	E E E E G G	L L L L V V	107	Q Q Q Q 108 E E	Q Q Q Q 109	L L L L 110 P P	N N N N 111 L L	D D D D 112 M M	L L L 113	E E E E	A A A A 115 D D	C C C C 116	V V V V 117	I I I I 118	Q Q Q Q Q Q 119 A
Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2	103	T T T T 104 V V V	E E E 105 G G G G	L L L L 106 V V V V V	107	Q Q Q Q 108 E E E	Q Q Q Q T T T T T	L L L 110 P P P	N N N 111 L L L L	D D D D D D M M M M M	L L L 113	E E E 114	A A A 115 D D D D	C C C C 116 S S S	V V V V 117 I I I I I I	I I I I L L L L L	Q Q Q Q Q A A A A A A A A A A A A A A A
Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3	103	T T T 104 V V V V V	E E E 105 G G G	L L L 106 V V V V	107	Q Q Q Q Q 108 E E E E E E E Z 25 Q	Q Q Q Q 109 T T T T T T 126 R	L L L 110 P P P P P P	N N N N 1111 L L L L L L T 228	D D D D 112 M M M M M M M M M M M M M M M M M M	L L L 113 X 3 2 2 130	E E E E 114 E E E E E E E E E E E E E E	A A A A D D D D D D D D	C C C C C S S S S S S S S S S S S S S S	V V V V 117 I I I I I I I	I I I I 118 L L L L L K	Q Q Q Q Q 1119 A A A A A A A A
Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1	103	T T T T V V V V V V T 121	E E E E 105 G G G G G K K K	L L L L 106 V V V V V V V Y	107 :: :: :: :: :: :: :: :: :: :: :: :: ::	Q Q Q Q 108 E E E E E E Q Q Q	Q Q Q Q Q T T T T T T T T T T R R R	L L L L 110 P P P P P T 127	N N N N N 111 L L L L L T T T T	D D D D D D D D D D D D D D D D D D D	L L L 113 %	E E E E E E E E E E E E E E E E E E E	A A A A 115 D D D D D D	C C C C T 116 S S S S S S S S E E E	V V V V 117 I I I I I K K	I I I I 118 L L L L L K K K	Q Q Q Q Q Q 1119 A A A A A A A Y Y Y
Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3	103 2 3 3 5 120 V	T T T T T V V V V V V V T 121	E E E E E E G G G G G K K	L L L L 106 V V V V V V V	107 107 108 1124 F	Q Q Q Q 108 E E E E E E Z Q Q	Q Q Q Q Q T T T T T T T T T T T T T T T	L L L L 110 P P P P P I 127	N N N N 1111 L L L L L T T T	D D D D D M M M M M M M L29 L L	L L L 113	E E E E E E E E E E E E E E E E E E E	A A A A A 115 D D D D D D D D D D D D D D D D D D	C C C C C S S S S S S S S S S S S S S S	V V V V 117 I I I I I I K	1 1 1 1 1 1 1 L L L L L L K K K	Q Q Q Q Q 1119 A A A A A A A Y Y
Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3	103	T T T T V V V V V V T 121	E E E E 105 G G G G G K K K K	L L L L 106 V V V V V V V Y	107 2 124 F F F	Q Q Q 108 E E E E E Q Q Q Q	Q Q Q Q 109 T T T T T R R R	L L L L 110 P P P P P P I 127 I I I	N N N N N 111 L L L L L T T T T	D D D D D D D D D D D D D D D D D D D	L L L 113 2 3 3 3 4 7 7 7 7	E E E E 114 E E E E E E E E E E E E E E	A A A A 115 D D D D D D D D D D D D D D D D D D	C C C C T 116 S S S S S S S S S S S S S S S S S S	V V V V 117 I I I I I K K K K	I I I I 118 L L L L L K K K	Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q
Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3	103 3 120 V V V V V	T T T T T V V V V V V T 121	E E E E E I 105 G G G G G K K K K K K K K K K K C I 39 C	L L L L 106 V V V V V V V 123 Y Y Y Y Y Y Y	107 124 F F F F F F F	Q Q Q Q 108 E E E E E Q Q Q Q Q Q 142 E	Q Q Q Q Q Q T T T T T T T 126 R R R R R R R R R N T T T T T T T T T T	L L L L 110 P P P P P P 127 I I I I I	N N N N N N 1111 L L L L L T T T T T T T T T T T T	D D D D D D D D D D D D D D D D D D D	L L L 113 X 3 2 2 3 2 4 130 Y Y Y Y Y Y Y	E E E E I 114 E E E E E E E E E E E E E E E E E E	A A A A 115 D D D D D T T 132	C C C C C S S S S S S S S S S S S S S S	V V V V V 117 I I I I I I I I I I I I I I I I I I	1 1 1 1 1 1 1 1 L L L L L L L L L L T 1 1 1 5 C K K K K K K K K K K K K K K K K K K	Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q
Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3	103 120 V V V V V V V S S	T T T T T T V V V V V V T 121	E E E E I 105 G G G G G I 22 K K K K K K K K K C C C C	L L L L 106 V V V V V V 123 Y Y Y Y Y Y A A	107 124 F F F F F F W W	Q Q Q 108 E E E E E Q Q Q Q 142 E E E E	Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q	L L L L 110 P P P P P P 127 I I I I V V V	N N N N N N 111 L L L L L 128 T T T T T T T T T R R R R	D D D D D D D D D D D D D D D D D D D	L L L 113 3 3 3 3 3 130 Y Y Y Y Y Y Y E E	E E E E I 114 E E E E E I 114 E E E E E E E E E E E E E E E E E E	A A A A A A 115 D D D D D D D D D D D D D D D D D D	C C C C C S S S S S S S S S S S S S E E E E	V V V V V 117 I I I I I I I I I I I I I I I I I I	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q
Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3	103 120 V V V V V V V V V	T T T T T T V V V V V V T 121	E E E E I 105 G G G G G K K K K K K K K K K C C C	L L L L 106 V V V V V V V 123 Y Y Y Y Y Y Y A A A A A A A A A A A A	107 124 F F F F F F F W	Q Q Q Q 125 Q Q Q Q 142 E E	Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q	L L L L 110 P P P P P P 127 I I I I I V V V	N N N N N N 111 L L L L L T T T T T T T T T R R	D D D D D D D D D D D D D D D D D D D	L L L 113 % 3 3 130 Y Y Y Y Y Y Y Y E E	E E E E I 114 E E E E E I 114 E E E E E E E E E E E E E E E E E E	A A A A 115 D D D D D D M M	C C C C C S S S S S S S S S S S S S S S	V V V V 117 I I I I I I I I I I I I I I I I I I	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q
Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3	103 2 120 V V V V V V V S S S	T T T T 104 V V V V V 121 138 P P P P	E E E E E I 105 G G G G G G K K K K K K K C C C C C	L L L L 106 V V V V V V 123 Y Y Y Y Y Y A A A	107 124 F F F F F F F W W W	Q Q Q 108 E E E E E E E E E E E E E E E E E E E	Q Q Q Q 109 T T T T T 126 R R R R R V V V V	L L L L 110 P P P P P P 127 I I I I I V V V V	N N N N 111 L L L L L L T T T T T T T R R R R R R R	D D D D D D D D D D D D D D D D D D D	L L L 113 2 3 3 130 Y Y Y Y Y Y E E E E	E E E E I 114 E E E E E E E E E E E E E E E E E E	A A A A A A A D D D D D D D D D D D D D	C C C C C S S S S S S S S S S S S S S S	V V V V V 117 I I I I I I I I I I I I I I I I I I	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q
Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3	103 120 V V V V V 137 S S S S S	T T T T T T T T T T T T T T T T T T T	E E E E E E E E E E E E E E E E E E E	L L L L 106 V V V V V V 123 Y Y Y Y Y Y Y 140 A A A A	107 124 F F F F F F F F F F F F F F F F F F F	Q Q Q 108 E E E E E E E E E E E E E E E E E E E	Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q	L L L L 110 P P P P P 127 I I I I I V V V V V	N N N N N N N N N N N N N N N N N N N	D D D D D D D D D D D D D D D D D D D	L L L 113 3 3 3 3 3 3 3 3 3 4 7 7 7 7 7 7 7 7 7	E E E E E I 114 I L L L L L L L I 148 I I I I I I I I I I I I I I I I I I I	A A A A A A A A A A A A A A A A A A A	C C C C C S S S S S S S S S S S S S S S	V V V V V 117 I I I I I I I I I I I I I I I I I I	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q
Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3	103 3 3 120 V V V V V V T 37 S S S S S	T T T T T T T T T T T T T T T T T T T	E E E E E E G G G G G G K K K K K 139 C C C C C C C C 1566	L L L L 106 V V V V V V 123 Y Y Y Y Y Y Y 140 A A A A	107 124 F F F F F F F F F F F F F F F F F F F	Q Q Q 108 E E E E E E E E E E E E E E E E E E E	Q Q Q Q 109 T T T T T 126 R R R R R V V V V V 160	L L L L 110 P P P P P P 127 I I I I V V V V	N N N N N N 1111 L L L L L T T T T T T 145 R R R R R R R R R R R R R R R R R R R	D D D D D D D D D D D D D D D D D D D	L L L 113 2 3 3 130 Y Y Y Y Y Y E E E E E	E E E E E I 1 1 4 8 I I I I I I I I I I I I I I I I I I	A A A A A A A B D D D D D D D D D D D D	C C C C C S S S S S S S S S S S S S S S	V V V V V 117 I I I I I I I I I I I I I I I I I I	1 1 1 1 1 1 1 L L L L L L L S K K K K K K K K K K K K	Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q
Alpha 21a HY-1 HY-2 HY-3 Alpha 2c Alpha 21a HY-1 HY-2 HY-3	103 120 V V V V V 137 S S S S 154 L L	T T T T T T T T T T T T T T T T T T T	E E E E E E E S G G G G G G G C C C C C C C C C C C C	L L L L 106 V V V V V V V 123 Y Y Y Y Y Y Y 140 A A A A A	107 124 F F F F F F F F F F F F F F F F F F F	Q Q Q Q 108 E E E E E E E E E E E E E E E E E E E	Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q	L L L L 110 P P P P P 127 I I I I I V V V V V	N N N N N N N N N N N N N N N N N N N	D D D D D D D D D D D D D D D D D D D	L L L 113 3 3 3 3 3 3 3 3 4 7 7 7 7 7 7 7 7 7 7	E E E E E I 114 I L L L L L L I 148 I I I I I I I I I I I I I I I I I I I	A A A A A A A A A A A A A A A A A A A	C C C C C S S S S S S S S S S S S S S S	V V V V V 117 I I I I I I I I I I I I I I I I I I	1 1 1 1 1 1 1 L L L L L L L S K K K K K K K K K K K K	Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q